

In the Claims

Please amend the claims as follows. Insertions and deletions are indicated by underlining (or double bracketing) and strikethrough, respectively.

1. (Currently amended) A polypeptide or polypeptide construct comprising:
at least one single domain antibody directed against any of von Willebrand Factor (vWF), ~~vWF~~
~~A1 domain, A1 domain of activated vWF, vWF A3 domain, gpIb, or collagen.~~
2. (Currently amended) A polypeptide or polypeptide construct according to claim 1,
~~further comprising at least one~~ two or more single domain ~~antibody~~ antibodies directed against
vWF ~~one or more serum proteins.~~
- 3.-21. (Canceled)
22. (Currently amended) A composition comprising a polypeptide or polypeptide construct
according to claim 1 and a pharmaceutically acceptable vehicle.
- 23.-33. (Canceled)
34. (New) A polypeptide or polypeptide construct according to claim 1, in which the at least
one single domain antibody directed against vWF is directed against vWF A1 domain, the A1
domain of activated vWF or the vWF A3 domain.
35. (New) A polypeptide or polypeptide construct according to claim 1 comprising two or
more single domain antibodies, in which at least one single domain antibody is directed against
vWF A1 domain, the A1 domain of activated vWF or the vWF A3 domain.
36. (New) A polypeptide or polypeptide construct according to claim 1, wherein the at least
one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to
7, 23 to 31, and 62 to 65, or to:

an homologous sequence of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 with a sequence identity of more than 70% with the parent sequence; or

a functional portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that maintains the interaction with the target with affinity of 1×10^{-6} M or better; or

a functional portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with the target.

37. (New) A polypeptide or polypeptide construct according to claim 1, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65, or to:

an homologous sequence of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation at high shear (1600 s^{-1}) at $1 \text{ }\mu\text{g/ml}$ or at lower concentrations; or

a functional portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that maintains the interaction with the target with affinity of 1×10^{-6} M or better; or

a functional portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with the target.

38. (New) A polypeptide or polypeptide construct according to claim 1, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65, or to:

an homologous sequence of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is a) able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1 \text{ }\mu\text{g/ml}$ or at lower concentrations, and b) not able to inhibit 50% of platelet aggregation under low shear (300 s^{-1}) condition at $10 \text{ }\mu\text{g/ml}$ or at lower concentrations; or

a functional portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that maintains the interaction with the target with affinity of 1×10^{-6} M or better; or

a functional portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with the target.

39. (New) A polypeptide or polypeptide construct comprising at least one single domain antibody directed against von Willebrand Factor, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NO: 3, or to an homologous sequence of SEQ ID NO: 3 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1\text{ }\mu\text{g/ml}$ or at lower concentrations.

40. (New) A polypeptide or polypeptide construct comprising at least one single domain antibody directed against von Willebrand Factor, wherein the at least one single domain antibody corresponds to a sequence represented by SEQ ID NO: 5, or to an homologous sequence of SEQ ID NO: 5 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1\text{ }\mu\text{g/ml}$ or at lower concentrations.

41. (New) A polypeptide or polypeptide construct comprising at least one single domain antibody directed against von Willebrand Factor, wherein the at least one single domain antibody corresponds to a sequence represented by SEQ ID NO: 7, or to an homologous sequence of SEQ ID NO: 5 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1\text{ }\mu\text{g/ml}$ or at lower concentrations.

42. (New) A polypeptide or polypeptide construct comprising two or more single domain antibodies directed against von Willebrand Factor; and

wherein the two or more single domain antibodies correspond to a sequence represented by any of SEQ ID NO: 3, or to an homologous sequence of SEQ ID NO: 3 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is

able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1\text{ }\mu\text{g/ml}$ or at lower concentrations, or

wherein the two or more single domain antibodies correspond to a sequence represented by SEQ ID NO: 5, or to an homologous sequence of SEQ ID NO: 5 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1\text{ }\mu\text{g/ml}$ or at lower concentrations, or

wherein the two or more single domain antibodies correspond to a sequence represented by SEQ ID NO: 7, or to an homologous sequence of SEQ ID NO: 7 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at $1\text{ }\mu\text{g/ml}$ or at lower concentrations.

43. (New) A polypeptide or polypeptide construct according to claim 1 in which at least one single domain antibody is a VHH domain.

44. (New) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a VHH domain comprising an amino acid at position 45 according to the Kabat numbering that is selected from the group consisting of glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, tyrosine, tryptophan, methionine, serine, threonine, asparagine, and glutamine.

45. (New) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a VHH domain comprising an amino acid at position 103 according to the Kabat numbering selected from the group consisting of arginine, serine or an uncharged residue, optionally glycine.

46. (New) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a VHH domain that is obtained by immunising a camel and obtaining hybridomas therefrom, or by cloning a library of single domain antibodies and subsequently selecting the VHH using phage display.

47. (New) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is humanized.

48. (New) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a humanized VHH domain.

49. (New) A polypeptide or polypeptide construct according to claim 48, in which at least one single domain antibody is humanized by replacing one or more of the *Camelidae* amino acids by their human counterparts as found in a human consensus sequence.

50. (New) A polypeptide or polypeptide construct according to claim 48, in which at least one single domain antibody is humanized by replacing any of the following residues either alone or in combination: FR1 positions 1, 5, 28 and 30, the hallmark amino acids at FR2 positions 37, 44, 45 and 47, FR3 positions 74, 75, 76, 83, 84, 93 and 94 and FR4 positions 103, 104, 108 and 111, wherein the numbering of the positions is according to the Kabat numbering.

51. (New) A polypeptide or polypeptide construct according to claim 42 that comprises one or more single domain antibodies directed against the A1 domain of vWF.

52. (New) A polypeptide or polypeptide construct according to claim 42, in which the two or more single domain antibodies are of the same sequence.

53. (New) A polypeptide or polypeptide construct according to claim 42, in which the C-terminal end of the first single domain antibody is linked to the N-terminal end of the next single domain antibody.

54. (New) A polypeptide or polypeptide construct according to claim 42, wherein said polypeptide or polypeptide construct is not able to inhibit 50% or more of platelet aggregation under low shear (300 s^{-1}) condition at $10\text{ }\mu\text{g/ml}$ or at lower concentrations.

55. (New) A composition comprising a polypeptide or polypeptide construct according to claim 22, wherein the composition is formulated for oral, parenteral, intra-nasal, inhalation, intravenous, intramuscular, topical or subcutaneous administration.